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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,073	02/05/2004	Francoise Bono-Combie	IVD001000 US DIV I	6033

5487 7590 04/19/2006

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EXAMINER	
BALLS, ROBERT J	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,073	BONO-COMBIE ET AL.	
	Examiner	Art Unit	
	James Balls	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 23 is pending.

2. This application is a divisional of 10/044,223 filed November 20, 2001, now U.S. Patent No. 6,693,118, which is a divisional of Application Serial No. 09/423,884 filed on April 10, 2000, now U.S. Patent No. 6,342,505, which is a 371 of PCT/FR98/01000 filed on May 20, 1998.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 23 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 23 is drawn to a method of inhibiting apoptosis in a patient for the treatment of prion diseases. The specification on page 13, lines 4-6 explain that the phrase, "treatment of diseases" is understood as meaning both the treatment and the prevention of the diseases. However, this definition does not resolve the ambiguity associated with the statement, "treatment of prion diseases," as its' meaning is subject to multiple interpretations. For instance, the phrase may refer to preventing cells from becoming infected with a prion protein, or the phrase may refer to method of regenerating a prion-infected cell into a healthy prion-free cell, or the phrase

may refer to treating the symptoms associated with prion infection such as prolonging brain function.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

4. Claim 23 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. To satisfy the written description requirement, a specification must describe the claimed invention in sufficient detail that one skilled in the art would reasonably conclude that the inventor had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); MPEP 2163. Applicants' claim a method of treating a prion disease. The term "prion" is listed once on page 12, line 32 in the specification amongst a laundry list of no less than seventy-five other diseases, many of which are broad disease classes that further include numerous sub-diseases. The specification does not include an actual reduction to practice. Instead, the specification states that "the representative compounds of formula (I) showed an increase in the levels of TGF-β1" on page 11, lines 17-18. However, the specification does not show how increased

levels of TGF-β1 relate to treating a prion disease. For instance, there is no disclosed correlation between structure and function. Also, the functional characterstics of increasing TGF-β1 levels to treat prion diseases is not recognized in the art. Whether applicants had possession of the claimed invention is determined by one of ordinary skill in the art. Therefore, the analysis turns to the art to assess the perspective of the skilled artisan. The art explains that the exact mechanism of neurodegeneration associated with prion diseases is unknown and that currently there are no therapies for their treatment. Tashiro et al., *Differential Expression of Transforming Growth Factor-β Isoforms in Human Prion Diseases*, NEUROPATH. APPL. NEURO., 24:284-292 (1998). Furthermore, a definite diagnosis of a prion disease requires a brain biopsy or an autopsy, procedures rarely carried out because they do not help the patient. See The Center for Healthy Aging's Helpguide online at http://www.helpguide.org/elder/creutzfeldt_jakob.htm. The art is void of any information to support a method for treating a prion disease. Based on the limited disclosure in the specification, the absence of working examples, and state of the prior art, one of ordinary skill in the art cannot conclude that applicants had possession of the invention as claimed.

5. Claim 23 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Courts rely on the following factors set out in *In re Wands* to determine whether undue experimentation is required to practice a claimed invention, i.e. whether the claimed invention is enabled: (a) The breadth of the claims; (b) The nature of the invention and predictability in the art; (c) The state of the prior art; (d) The level of one of ordinary skill; (e) The amount of direction and existence of working examples; and (f) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. *Id.* The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407.

The analysis is applied to the instant case.

(a) The claim is drawn to a method of inhibiting apoptosis to treat prion diseases.

(b) The invention is physiological in nature as it is directed toward pharmaceuticals and treating diseases with those pharmaceuticals, an art which is highly unpredictable. "[T]he scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ

18, 24 (CCPA 1970). In the highly unpredictable pharmaceutical art, the required disclosure is greater than for the disclosure of an invention involving predictable factors such as mechanical or electrical elements. *In re Vaeck*, 20 USPQ 2d 1438 (CAFC 1991).

(c) The state of the prior art shows that the exact mechanism by which prion diseases cause neurodegeneration is unknown. Tashiro et al., page 284, last sentence of the first paragraph. Tashiro et al. also explain that they found no distinct clinical or pathological findings linking TGF-β1 and prion diseases. Tashiro et al., page 287, first column, last full sentence. The prior art fails to show a correlation between TGF-β1 and prion diseases.

(d) The level of skill required to practice a method of treating a prion disease is extremely high based on the limited understanding of prion-disease pathology, the difficulty in diagnosing the disease, and absence of effective therapies.

(e) The specification contains no working examples demonstrating a method for treating a prion disease. Instead, the term "prion" is listed once on page 12, line 32 in the specification amongst a laundry list of no less than seventy-five other diseases, many of which are broad disease classes that further include numerous sub-diseases.

(f) The quantity of experimentation necessary to make or use the disclosed invention is high, based on the unpredictability of the art, the limited guidance in the specification, and the lack of direction and working examples. Therefore, a person of ordinary skill in the art would be subjected to undue experimentation in order to make and use the invention rendering the claim unpatentable.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Balls whose telephone number is (571) 272-7997. The examiner can normally be reached on Mon - Fri 8:00am - 4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cecelia Tsang

R. James Balls
Examiner
Art Unit 1625

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